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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

CHUNDURU, SURYAPRABHA

ART UNIT	PAPER NUMBER
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1637

DATE MAILED: 04/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/885,731

Applicant(s)

ERIKSON ET AL.

Examiner

Suryaprabha Chunduru

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 05 February 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-5 and 7-55 is/are pending in the application.
- 4a) Of the above claim(s) 28 and 30-55 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-5, 7-27 and 29 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

1. Applicants' response to the office action filed on February 5, 2004 has been entered.
2. This application is filed on June 20, 2001 and claims priority to US Patent application Nos. 09/664,827, filed on September 19, 2000, 09/613,263 filed on July 10, 2000, and 09/468,679, filed on December 21, 1999.
3. Claims 1-5, 7-27 and 29 are considered for examination. Claims 28, 30-55 were withdrawn from consideration pursuant to restriction requirement.

Response to Arguments

4. Applicant's response to the office action (Paper No.16) is fully considered and is found not persuasive.
5. The following is the rejection made in the previous office action under 35 USC 103 (a):

Claims 1-5, 7-27, 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over George Jr. (USPN. 5,451,502) in view of McGavin et al. (J. Mol. Graphics, Vol. 7, pages 218-232, 1989).

George Jr. teaches method for creating a nucleic acid multiplex of claims 1, 2, 4, and 29 (see column 3, lines 49-67, column 4, lines 1-35) wherein the method comprises

(a) creating a mixture comprising water (buffer), a Watson-Crick duplex (double-stranded nucleic acid) (see column 3, lines 49-61, column 4, lines 1-16), a number of single-stranded mixed base sequence molecules (probe or oligonucleotide containing at least a nucleobase sequence) (see column 3, lines 49-58), at least one accelerator agent (label) and

(b) incubating the reaction mixture to form said multiplex (see column 4, lines 10-16).

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George Jr. also teaches that the probe comprises 5-57 nucleotides and target contains unlimited number of bases (see column 6, lines 1-24, column 9, lines 11-23);

With regard to claims 9-11, George Jr., teaches that the method comprises water, accounting for volume basis of the mixture, ranging from 50% to 90% (see column 9, lines 45-51);

With regard to claims 12-14, George Jr. teaches that the method was carried out at temperatures ranging from 2-60⁰ C and pH of the hybridization buffer of about 5 to about 9 (see column 8, lines 34-53, column 10, lines 4-22, column 11, lines 65-68, column 12, lines 1-61);

With regard to claims 15-17, George Jr., teaches that the method comprises cations such as Na⁺, Mg²⁺, in a concentration ranging 50 mM to 100mM for NaCl, 5-10mM for MgCl₂ (see column 8, lines 35-53, column 9, lines 36-51);

With regard to claims 21-22, George Jr. teaches a flurophore label fluorescence, chemiluminescence label comprising rodhamine and fluorescein (see column 7, lines 1-19); A flurophore label with detectable marker using an atom, an inorganic radical (comprise monovalent cation), heavy metal (transition metals) (divalent or valency grater than 1), biotin and like (see column 6, lines 25-46);

With regard to claims 24-27, the accelerator agent is an organic liquid soluble in water (DMSO, formamide, ethylene glycol, glycerine) (see column 9, lines 40-44);

However George Jr. did not specifically teach that the each strand of said multiplex structure (probe-target complex) is related to all other strands of the multiplex by Watson-Crick base-pairing rules.

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McGavin et al. teach formation of a multiplex structure of claims 1-5, 7-27, 29, wherein McGavin et al. disclose a multiplex structure comprising a first, a second, a third and a fourth sequence of nucleobases wherein four strands interact specifically with each other forming a multiplex structure through Watson-Crick pairing (see page 226, column 1, paragraphs 2-4) in which Watson-Crick duplexes are paired specifically about a dyad axis coincident with a common long molecular axis and with major grooves in continuous and specific contact (see page 230, column 1, paragraphs 1-3, page 225, column 1, paragraph 2, column 2, paragraph 3).

McGavin et al. teach that the multiplex structure comprises an artificial or synthetic quadruplex (see page 228, column 1, paragraphs 2-4); the multiplex structure comprises a nucleic acid (DNA and RNA) (see page 225, column 2, paragraph 3); in the multiplex structure any one strand alternates between two strands in anti-parallel orientation (see page 220, color plate 3a and 3b, page 228, column 2, paragraphs 3-8); Watson-Crick duplexes are paired specifically about a dyad axis coincident with a common long molecular axis and with major grooves in continuous and specific contact indicating major groove of first-second strand duplex is placed in the major groove of third-fourth strand duplex (see page 230, column 1, paragraphs 1-3, page 225, column 1, paragraph 2, column 2, paragraph 3);

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of forming or creating a multiplex as taught by George Jr. with the inclusion of Watson-Crick base pairing forming model as taught by McGavin et al. in order to obtain the invention as a whole. An ordinary artisan would have motivated to have added the structural stability of Watson-Crick base pairing of nucleic acid strands in a multiplex structure to the method of George Jr., because McGavin et al. taught Watson-Crick

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kind of base pairing as a strong specific interaction between complementary strands and its growing significance in genetic recombination or specificity of interaction between strands. Therefore an ordinary artisan would have recognized the expected benefits of stability of Watson-Crick kind of base pairing structures and would have motivated to add the limitation to the method of forming a multiplex as taught by George Jr. to obtain a more stable multiplex structure.

Response to arguments:

With regard to the above rejection, Applicants' arguments have been fully considered and found not persuasive. Applicants argue that there is no motivation to employ the purely theoretical teachings of McGavin to modify the primary reference, George since the prior art McGavin discloses a theoretical model for quadruplex nucleic acid sequences based on the Watson-Crick tetrads and McGavin is a non-enabling art. These arguments are fully considered and found not persuasive because in previous office action Applicants submitted the same reference to show that the Watson-Crick base pairing is enabled by computer graphic structures disclosed by the McGavin reference. Contradictory to this, presently, Applicants argue that the prior art is non-enabling prior art. Examiner notes that one of ordinary skill in the art would rely on the McGavin reference for the structure as claimed in the instant invention because Applicants did not show any crystallographic data to show how the instantly claimed structure is formed with Watson-Crick base pairing involving more than two strands. It is noted in MPEP 2121.04 "Pictures and drawings may be sufficiently enabling to put the public in the possession of the article pictured. Therefore, such an enabling picture may be used to reject claims to the article. However, the picture must show all the claimed structural features and how they are put

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together. *Jockmus v. Leviton*, 28 F.2d 812 (2d Cir. 1928). See also MPEP § 2125 for a discussion of drawings as prior art. Thus the computer graphic structure disclosed by McGavin is considered as enabling art.

Further Applicants then argues that the invention is "obvious to try" but lacks a reasonable expectation of success. The legal standard for "reasonable expectation of success" is provided by caselaw and is summarized in MPEP 2144.08, which notes "obviousness does not require absolute predictability, only a reasonable expectation of success; i.e. , a reasonable expectation of obtaining similar properties. See , e.g. , *In re O'Farrell* , 853 F.2d 894, 903, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988)." In this factual case, there is express suggestion in the prior art McGavin et al. which expressly teaches the stable-structure can be achieved by Watson-Crick bases-pairing. The is sufficient for a reasonable expectation of success. The MPEP cites *In re O'Farrell*, which notes regarding "obvious to try" at page 1682, that, In some cases, what would have been "obvious to try" would have been to vary all parameters or try each of numerous possible choices until one possibly arrived at a successful result, where the prior art gave either no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful. E.g. , *In re Geiger* , 815 F.2d at 688, 2 USPQ2d at 1278; *Novo Industri A/S v. Travenol Laboratories, Inc.* , 677 F.2d 1202, 1208, 215 USPQ 412, 417 (7th Cir. 1982); *In re Yates* , 663 F.2d 1054, 1057, 211 USPQ 1149, 1151 (CCPA 1981); *In re Antonie* , 559 F.2d at 621, 195 USPQ at 8-9. In others, what was "obvious to try" was to explore a new technology or general approach that seemed to be a promising field of experimentation, where the prior art gave only general guidance as to the particular form of the claimed invention or how to achieve it. *In re Dow Chemical Co.* , 837 F.2d, 469, 473, 5

USPQ2d 1529, 1532 (Fed. Cir. 1985); *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1380, 231 USPQ 81, 90-91 (Fed. Cir. 1986), cert. denied, 107 S.Ct. 1606 (1987); *In re Tomlinson*; 363 F.2d 928, 931, 150 USPQ 623, 626 (CCPA 1966).

Further in response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, specific motivation is provided in the rejection above, which notes that An ordinary artisan would have motivated to have added the structural stability of Watson-Crick base pairing of nucleic acid strands in a multiplex structure to the method of George Jr., because McGavin et al. taught Watson-Crick kind of base pairing as a strong specific interaction between complementary strands and its growing significance in genetic recombination or specificity of interaction between strands. Therefore an ordinary artisan would have recognized the expected benefits of stability of Watson-Crick kind of base pairing structures and would have motivated to add the limitation to the method and composition of binding assay as taught by George Jr to obtain a more stable multiplex structure. Therefore the rejection is maintained herein.

Conclusion

No claims are allowable.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suryaprabha Chunduru whose telephone number is 571-272-0783. The examiner can normally be reached on 8.30A.M. - 4.30P.M, Mon - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion reached on 571-272-0782. The fax phone numbers for the organization where this application or proceeding is assigned are 703872-9306 for regular communications and - for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.


Suryaprabha Chunduru
April 21, 2004


JEFFREY FREDMAN
PRIMARY EXAMINER
